

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 13 December 2000 (13.12.00)	Applicant's or agent's file reference 11137/04803
International application No. PCT/US00/13389	Priority date (day/month/year) 20 May 1999 (20.05.99)
International filing date (day/month/year) 15 May 2000 (15.05.00)	
Applicant DIXON, Richard, A. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 03 November 2000 (03.11.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 Form PCT/IB/331 (July 1992)	Authorized officer Diana Nissen Telephone No.: (41-22) 338.83.38
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US0013389

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

HANSEN, Eugenia, S.
Sidley Austin Brown & Wood
Suite 3400
717 North Harwood
Dallas, TX 75201
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 18 octobre 2001 (18.10.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 11137/04803	International filing date (day/month/year) 15 mai 2000 (15.05.00)
International application No. PCT/US00/13389	

1. The following indications appeared on record concerning:

☐ the applicant
 ☐ the inventor
 ☒ the agent
 ☐ the common representative

Name and Address

HANSEN, Eugenia, S.
Sidley & Austin
Suite 3400
717 North Harwood
Dallas, TX 75201
United States of America

State of Nationality

State of Residence

Telephone No.

214 981 3300

Facsimile No.

214 981 3400

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person
 ☒ the name
 ☐ the address
 ☐ the nationality
 ☐ the residence

Name and Address

HANSEN, Eugenia, S.
Sidley Austin Brown & Wood
Suite 3400
717 North Harwood
Dallas, TX 75201
United States of America

State of Nationality

State of Residence

Telephone No.

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Facsimile No.

214 981 3400

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office
 ☐ the designated Offices concerned
☐ the International Searching Authority
 ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority
 ☐ other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Dorothee MÜLHAUSEN

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 11137/04803	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/13389	International filing date (day/month/year) 15/05/2000	(Earliest) Priority Date (day/month/year) 20/05/1999
Applicant THE SAMUEL ROBERTS NOBLE FOUNDATION, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of Invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1

☐ None of the figures.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/82 C12N15/29 C12N9/10 C07K16/16 A01H5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, BIOSIS, WPI Data, PAJ, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ✓	HE XIAN-ZHI ET AL: "Stress responses in alfalfa (Medicago sativa L). XXII. cDNA cloning and characterization of an elicitor-inducible isoflavone 7-O-methyltransferase" PLANT MOLECULAR BIOLOGY, NL, NIJHOFF PUBLISHERS, DORDRECHT, vol. 36, no. 1, 1 January 1998 (1998-01-01), pages 43-54, XP002139377 ISSN: 0167-4412 cited in the application page 52, right-hand column -page 53, left-hand column	32-35
X ✓	WO 93 23069 A (KELLY GRAHAM EDMUND) 25 November 1993 (1993-11-25) page 9, examples, claims ----- -/-	40-43



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

22 September 2000

Date of mailing of the international search report

06/10/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Holtorf, S

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>✓ US 4 704 400 A (MILLER DOUGLAS K ET AL) 3 November 1987 (1987-11-03) the whole document</p>	40-43
A	<p>✓ DATABASE EMBL SEQUENCE LIBRARY 'Online! 5 November 1997 (1997-11-05) HE, X., ET AL. : "Stress responses in alfalfa (Medicago sativa L). XXII. cDNA cloning and characterization of an elicitor-inducible isoflavone 7-O-methyltransferase" XP002148151 accession no. U97125</p>	
A	<p>✓ DIXON R A ET AL: "PROSPECTS FOR THE METABOLIC ENGINEERING OF BIOACTIVE FLAVONOIDS AND RELATED PHENYLPROPANOID COMPOUNDS" ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, SPRING ST., NY, US, vol. 439, 1998, pages 55-66, XP000929350 ISSN: 0065-2598 page 61 -page 62</p>	
P, X	<p>✓ DIXON, R.A. ET AL.: "molecular controls for isoflavonoid biosynthesis in relation to plant and human health" PHYTOCHEMICALS IN HUMAN HEALTH PROTECTION, NUTRITION, AND PLANT DEFENCE: KLUWER ACADEMIC/PLENUM PUBLISHERS. EDITED BY J.T. ROMEO. NEW YORK ISBN: 0-306-46203-6, September 1999 (1999-09), pages 133-159, XP000925618 last paragraph page 147</p>	1-5, 18-35, 44-51
E	<p>✓ WO 00 37656 A (DU PONT ; FADER GARY M (US); MCGONIGLE BRIAN (US); ODELL JOAN T (US) 29 June 2000 (2000-06-29) the whole document</p>	29, 31

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

US 00/13389

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9323069	A	25-11-1993	AU 683838 B	27-11-1997
			AU 4052593 A	13-12-1993
			BR 9306393 A	15-09-1998
			CA 2136233 A	25-11-1993
			EP 0656786 A	14-06-1995
			JP 7506822 T	27-07-1995
			NO 944435 A	18-11-1994
			NZ 252051 A	28-10-1996
			US 5830887 A	03-11-1998
US 4704400	A	03-11-1987	GB 2191944 A	31-12-1987
WO 0037656	A	29-06-2000	WO 0037652 A	29-06-2000

REPLACED BY
ART 34 AMBT

PATENT COOPERATION TREATY

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REC'D 15 OCT 2001

WIPO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 11137/04803		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/13389	International filing date (day/month/year) 15/05/2000	Priority date (day/month/year) 20/05/1999	
International Patent Classification (IPC) or national classification and IPC C12N15/82			
Applicant THE SAMUEL ROBERTS NOBLE FOUNDATION, INC. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 4 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the report.II <input type="checkbox"/> PriorityIII <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input checked="" type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input checked="" type="checkbox"/> Certain documents citedVII <input type="checkbox"/> Certain defects in the international applicationVIII <input type="checkbox"/> Certain observations on the international application			
Date of submission of the demand 03/11/2000		Date of completion of this report 11.10.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Zellner, E Telephone No. +49 89 2399 8427	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/13389

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-26 as originally filed

Claims, No.:

1-51 as originally filed

Drawings, sheets:

1/11-11/11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/13389

- ☐ the drawings, sheets:
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
- ☐ not complied with for the following reasons:
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☒ all parts.
- ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-38, 43-50
	No:	Claims	39-42
Inventive step (IS)	Yes:	Claims	4,5,11-14,16,17,19,20,24,25,27,28,30,31,33,34,37,38
	No:	Claims	1-3,6-10,15,18,22-23,26,29,32,35,36,43-50

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/13389

Industrial applicability (IA) Yes: Claims * 1-50
 No: Claims

2. Citations and explanations
 see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Reference is made to the following documents:

- D1: HE XIAN-ZHI ET AL: 'Stress responses in alfalfa (*Medicago sativa* L). XXII. cDNA cloning and characterization of an elicitor-inducible isoflavone 7-O-methyltransferase' PLANT MOLECULAR BIOLOGY, NL, NIJHOFF PUBLISHERS, DORDRECHT, vol. 36, no. 1, 1 January 1998 (1998-01-01), pages 43-54, XP002139377 ISSN: 0167-4412 cited in the application
- D2: WO 93 23069 A (KELLY GRAHAM EDMUND) 25 November 1993 (1993-11-25)
- D3: US-A-4 704 400 (MILLER DOUGLAS K ET AL) 3 November 1987 (1987-11-03)
- D4: WO 00 37656 A (DU PONT ;FADER GARY M (US); MCGONIGLE BRIAN (US); ODELL JOAN T (US) 29 June 2000 (2000-06-29)

Item V

1. D2 describes compositions comprising 4'-O-methylated isoflavonoid (page 9) which is administered as foodstuff (page 14, last paragraph).
The composition as such is known from D2 no matter how it is isolated or produced (see item VIII). The amount of 4'-O-methylated isoflavonoid is variable, no matter how it is isolated. Therefore it can also be present in a so called "increased" level in D2. The amount of 4'-O-methylated isoflavonoid in plants is thus not suitable to distinguish the composition from D2. In addition, there is no level defined in Claim 39.
Therefore the compositions of claims 39-42 are not novel.
2. D1 describes the DNA and amino acid sequence of alfalfa isoflavone 7-O-methyltransferase (Fig. 2) and its expression in *E. coli*. (page 46, left column, last paragraph- right column, 1st paragraph). Substrate and product specificity of IOMT expressed in *E. coli* is analysed in Table 1 (page 49). As depicted in said Table 1 of D1 7-O-methylated isoflavonoid compounds are produced in *E. coli*.
3. The closest prior art document is represented by D1 (see above).

In difference to the present application, D1 does not describe transgenic plants or any other cell exhibiting altered (increased or decreased) levels of **4'-O-methylated isoflavonoid** by expression of transgenic isoflavone-O-methyltransferase. In D1 E. coli cells producing recombinant isoflavone-O-methyltransferase is taught possessing 7' O-methyl transferase activity. The problem can thus be defined as the provision of a process leading to plants having an altered 4'-O-methylated isoflavonoid compound such as formononetin (Claim 19).

The solution as defined in the present claims 4, 5, 11-14 is the transformation of plants by a recombinant isoflavone O-methyltransferase gene such as defined in SEQ ID NO:1 in order to produce different levels of 4'-O-methylated isoflavonoid compound.

The solution is considered as not being obvious for the skilled person for the following reasons. In D1 it is taught that alfalfa isoflavone O-methyltransferase as used in the present application might have 4' activity *in vivo* (page 51, right column, last paragraph and page 52, right column, last paragraph - page 53, left column left, line 3). However, it is also stated that the isoflavone methyltransferase may not have 4'-O-methyltransferase activity *in vivo* (D1 page 53, left column, last paragraph, lines 1-5).

Therefore a skilled person would not obviously consider with a reasonable expectation of success that the known 7-O-methyltransferase of D1 can be used in plants (*in vivo*) in order to indeed enhance or inhibit the production of 4'-O-methylated isoflavonoid compounds (Example 4 of the present application).

Therefore inventive step can be acknowledged for the claims disclosing methods using the specific isoflavone O-methyltransferase as defined in SEQ ID: NO:1 such as Claims 16, 17, 19, 20, 24, 25, 27, 28, 30, 31, 33, 34, 37, 38, 40 and 41. However, for Claims 1-3, 6-10, 15, 18, 22-23, 26, 29, 32, 35, 36, 39, 43-50 not disclosing said specific isoflavone O-methyltransferase as defined in SEQ ID: NO: 1 the requirements of Article 33 (3) PCT are not fulfilled. Said claims disclose any isoflavone O-methyltransferase of any organism without being shown that there is indeed a solution i.e. that any of said isoflavone O-methyltransferase genes produce 4'-O-methylated isoflavonoid compound in target plant or even yeast or insect cells (Claims 32). Said claims do not provide

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/13389

a contribution to the prior D1, since they are only speculative such as the prior art D1 itself.

In conclusion, said claims are not considered as involving an inventive step. In addition, it is pointed out that from D1 it is derivable that isoflavone-O-methyltransferase purified from cell cultures possesses 7-IOMT activity. Thus the skilled person would expect that a plant transformed with said enzyme and isolated therefrom also possesses said activity. In consequence, Claim 29 does not involve an inventive step.

Item VI

Certain published documents (Rule 70.10)

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-A- 0 037 656	29.06.00	20.12.99	21.12.98

VIII

Claims 39-42 are formulated in terms of a "product by process". In the PCT contracting states no unified criteria exist concerning this type of claims. Before the EPO such claims, defined in terms of a product by process of manufacture are only admissible if the product as such fulfils the requirements of patentability, i.e. if the products are novel and inventive and if the product cannot be defined by true technical features (Article 6 PCT).

cell suspension cultures transformed with a DNA fragment comprising an isoflavone *O*-methyltransferase gene under the control of a suitable constitutive or inducible promoter.

30. The method of claim 29, wherein said fragment comprises SEQ ID NO:1.

31. The method of claim 29, wherein said fragment comprises a sequence exhibiting at least moderate hybridization with SEQ ID NO:1.

32. A method for the production of a 7-*O*-methylated isoflavonoid compounds comprising contacting a soluble or immobilized isoflavone *O*-methyltransferase enzyme with a non-methylated isoflavone precursors to said 7-*O*-methylated isoflavonoid compound, said enzyme produced by expression of a DNA fragment comprising the corresponding isoflavone *O*-methyltransferase gene in transgenic plants or a heterologous system.

33. The method of claim 32, wherein said heterologous system is selected from the group consisting of transfected bacterial, yeast and insect cells.

34. The method of claim 32 or 33, wherein said fragment comprises SEQ ID NO:1.

35. The method of claim 32 or 33, wherein said fragment comprises a sequence exhibiting at least moderate hybridization with SEQ ID NO:1.

36. An antiserum against 4'-*O*-methyltransferase used as a reagent for determining transgene expression of said 4'-*O*-methyltransferase in plants.

37. A method of increasing disease resistance in a target plant by transforming said target plant with a DNA fragment comprising an isoflavone *O*-methyltransferase gene, wherein said transformed plant exhibits increased levels of at least one 4'-*O*-methylated isoflavonoid when compared to levels of said 4'-*O*-methylated isoflavonoid in plants of the same species which do not comprise said DNA fragment.

38. The method of claim 37, wherein said fragment comprises SEQ ID NO:1.

39. The method of claim 37, wherein said fragment comprises a sequence exhibiting at least moderate hybridization with SEQ ID NO:1.

40. A composition comprising at least one 4'-*O*-methylated isoflavonoid suitable for administration as a food stuff, a nutritional supplement, an animal feed supplement, a nutraceutical, or a pharmaceutical, said 4'-*O*-methylated isoflavonoid isolated from at least a portion of a transgenic plant transformed with a DNA fragment comprising an isoflavone *O*-methyltransferase gene, wherein said transgenic plant exhibits increased levels of said 4'-*O*-methylated isoflavonoid when compared to levels of said 4'-*O*-methylated isoflavonoid in plants of the same species which do not comprise said DNA fragment.

41. The composition of claim 40, wherein said fragment comprises SEQ ID NO:1.

42. The composition of claim 40, wherein said fragment comprises a sequence exhibiting at least moderate hybridization with SEQ ID NO:1.

43. The composition of claim 40, 41 or 42, wherein said transgenic plant is a legume.

44. A transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said transgenic plant upon expression of said gene exhibits increased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

45. Seed from a transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits increased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

46. Progeny from a transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits increased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

47. Progeny from seed of a transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits increased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

48. A transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits decreased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

49. Seed from a transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits decreased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

50. Progeny from a transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits decreased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

51. Progeny from seed of a transgenic plant comprising at least one recombinant DNA sequence encoding a portion of an isoflavone *O*-methyltransferase gene, wherein said plant upon expression of said gene exhibits decreased levels of 4'-*O*-methylated isoflavonoid compounds when compared to levels of said 4'-*O*-methylated isoflavonoid compounds in plants of the same species which do not comprise said recombinant DNA sequence.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 00/13389

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/82 C12N15/29 C12N9/10 C07K16/16 A01H5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, BIOSIS, WPI Data, PAJ, STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HE XIAN-ZHI ET AL: "Stress responses in alfalfa (Medicago sativa L). XXII. cDNA cloning and characterization of an elicitor-inducible isoflavone 7-O-methyltransferase" PLANT MOLECULAR BIOLOGY, NL, NIJHOFF PUBLISHERS, DORDRECHT, vol. 36, no. 1, 1 January 1998 (1998-01-01), pages 43-54, XP002139377 ISSN: 0167-4412 cited in the application page 52, right-hand column -page 53, left-hand column ---	32-35
X	WO 93 23069 A (KELLY GRAHAM EDMUND) 25 November 1993 (1993-11-25) page 9, examples, claims ---	40-43
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

22 September 2000

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/13389

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 704 400 A (MILLER DOUGLAS K ET AL) 3 November 1987 (1987-11-03) the whole document	40-43
A	----- DATABASE EMBL SEQUENCE LIBRARY 'Online! 5 November 1997 (1997-11-05) HE, X., ET AL.: "Stress responses in alfalfa (Medicago sativa L). XXII. cDNA cloning and characterization of an elicitor-inducible isoflavone 7-O-methyltransferase" XP002148151 accession no. U97125	
A	----- DIXON R A ET AL: "PROSPECTS FOR THE METABOLIC ENGINEERING OF BIOACTIVE FLAVONOIDS AND RELATED PHENYLPROPANOID COMPOUNDS" ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, SPRING ST., NY, US, vol. 439, 1998, pages 55-66, XP000929350 ISSN: 0065-2598 page 61 -page 62	
P, X	----- DIXON, R.A. ET AL.: "molecular controls for isoflavonoid biosynthesis in relation to plant and human health" PHYTOCHEMICALS IN HUMAN HEALTH PROTECTION, NUTRITION, AND PLANT DEFENCE: KLUWER ACADEMIC/PLENUM PUBLISHERS. EDITED BY J.T. ROMEO. NEW YORK ISBN: 0-306-46203-6, September 1999 (1999-09), pages 133-159, XP000925618 last paragraph page 147	1-5, 18-35, 44-51
E	----- WO 00 37656 A (DU PONT ;FADER GARY M (US); MCGONIGLE BRIAN (US); ODELL JOAN T (US) 29 June 2000 (2000-06-29) the whole document	29, 31

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/13389

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9323069 A	25-11-1993	AU 683838 B	27-11-1997
		AU 4052593 A	13-12-1993
		BR 9306393 A	15-09-1998
		CA 2136233 A	25-11-1993
		EP 0656786 A	14-06-1995
		JP 7506822 T	27-07-1995
		NO 944435 A	18-11-1994
		NZ 252051 A	28-10-1996
		US 5830887 A	03-11-1998
US 4704400 A	03-11-1987	GB 2191944 A	31-12-1987
WO 0037656 A	29-06-2000	WO 0037652 A	29-06-2000